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**PATENT**  
Attorney Docket No. 224384  
Client Reference No.

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of:

Kasid et al.

Group Art Unit: 1635

Application No. 10/680,313

Examiner: James Schultz

Filed: October 6, 2003

For: GENE SHINC-1 AND DIAGNOSTIC  
AND THERAPEUTIC USES THEREOF

**INFORMATION DISCLOSURE STATEMENT**

Mail Stop  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Pursuant to 37 CFR 1.97 and 1.98, the references listed on the enclosed Form PTO-1449 and/or Substitute Form PTO-1449 ("Form 1449") are submitted for consideration by the Examiner in the examination of the above-identified patent application.

The full consideration of the references in their entirety by the Examiner is respectfully requested and encouraged. Also, it is respectfully requested that the references be entered into the record of the present application and that the Examiner place his or her initials in the appropriate area on the enclosed Form 1449, thereby indicating the Examiner's consideration of each of the references.

The submission of the references listed on the Form 1449 is for the purpose of providing a complete record and is not a concession that the references listed thereon are prior art to the invention claimed in the patent application. The right is expressly reserved to establish an invention date earlier than the above-identified filing date in order to remove any reference submitted herewith as prior art should it be deemed appropriate to do so.

Further, the submission of the references is not to be taken as a concession that any reference represents art that is relevant or analogous to the claimed invention. Accordingly, the right to argue that any reference is not properly within the scope of prior art relevant to an examination of the claims in the above-identified application is also expressly reserved.

The Information Disclosure Statement is being filed:

- ☒ **within** any one of the following time periods: (a) within three months of the filing date of a national application other than a continued prosecution application under 37 CFR 1.53(d); (b) within three months of the date of entry of the national stage as set forth in 37 CFR 1.491 of an international application; (c) before the mailing date

of a first Office Action on the merits; or (d) before the mailing of a first Office Action after the filing of a request for continued examination under 37 CFR 1.114.

- ☐ **after** (a), (b), (c) or (d) above, but before the mailing date of a final action under 37 CFR 1.113, a Notice of Allowance under 37 CFR 1.311, or an action that otherwise closes prosecution in the application, and includes *one* of:

☐ the Statement under 37 CFR 1.97(e) (see "Statement under 37 CFR 1.97(e)" below).

*or*

☐ the fee of \$180 set forth in 37 CFR 1.17(p) (see "Fees" below).

- ☐ **after** the mailing date of a final action under 37 CFR 1.113 or a Notice of Allowance under 37 CFR 1.311, or an action that otherwise closes prosecution in the application, and on or before payment of the issue fee, and includes the Statement under 37 CFR 1.97(e) (see "Statement under 37 CFR 1.97(e)" below), and the fee of \$180 as set forth in 37 CFR 1.17(p) (see "Fees" below).

- ☐ **after** the mailing date of a Notice of Allowance under 37 CFR 1.311, and on or before payment of the issue fee, and **within** thirty days of receiving each item of information contained in the Information Disclosure Statement, and includes the Statement under 37 CFR 1.704(d) (see "Statement under 37 CFR 1.704(d)" below), and the fee of \$180 as set forth in 37 CFR 1.17(p) (see "Fees" below).

NOTE: This is for original applications except applications for a design patent, filed on or after May 29, 2000, wherein a paper containing only an Information Disclosure Statement in compliance with 37 CFR 1.97 and 1.98 is being filed.

#### Copies of the References

- ☐ Copies of all of the references listed on the enclosed Form 1449 are enclosed herewith.

- ☒ Copies of U.S. patents and patent applications that are listed on the accompanying Form 1449 are not enclosed herewith. Copies of other references identified on the accompanying Form 1449 are enclosed herewith with the exception of Chin (March, 2002). A paper copy of the first 2 pages of the Chin reference is provided. The complete reference, which is approximately 10,000 pages, is provided on the enclosed CD-ROM, which is the format in which it was initially transmitted to us by a third party.

- ☒ Attached to each reference not in the English language is a concise explanation of the relevance pursuant to 37 CFR 1.98(a)(3). An English-language equivalent/patent, or an English-language abstract, or an English-language version of the search report or action by a foreign patent office in a counterpart foreign application indicating the degree of relevance found by the foreign office is being submitted in lieu of a concise explanation of the relevance pursuant to 37 CFR 1.98(a)(3).

- ☐ A copy of the foreign search report is enclosed herewith.

- ☐ The references listed on the enclosed Form 1449 were previously identified in the parent application(s) of the present application, and copies of the references were furnished at that time. Accordingly, additional copies of the references are not submitted herewith, so as not to burden the file with duplicate copies of references. The Examiner is respectfully requested to carefully review the references in accordance with the requirements set out in the Manual of Patent Examining Procedure. In accordance with 37 CFR 1.98(d), the details of the parent application(s) relied upon for an earlier filing date under 35 USC 120 in which copies of the references were previously furnished are set out below:

| U.S. APPLICATIONS |                  | Status ( <i>check one</i> ) |         |           |
|-------------------|------------------|-----------------------------|---------|-----------|
| U.S. APPLICATIONS | U.S. FILING DATE | PATENTED                    | PENDING | ABANDONED |
| 1.                |                  |                             |         |           |
| 2.                |                  |                             |         |           |
| 3.                |                  |                             |         |           |

**Statement under 37 CFR 1.97(e).**

- ☐ The **undersigned** hereby states that each item of information contained in the Information Disclosure Statement was first cited in any communication from a foreign patent office in a counterpart foreign patent application not more than three months prior to the filing of the Information Disclosure Statement.
- ☐ The **undersigned** hereby states that no item of information contained in the Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign patent application, and, to the knowledge of the undersigned after making reasonable inquiry, no item of information contained in the Information Disclosure Statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the Information Disclosure Statement.

**Statement under 37 CFR 1.704(d)**

- ☐ The **undersigned** hereby states that each item of information contained in the Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart application and that this communication was not received by any individual designated in 37 CFR 1.56(c) more than thirty days prior to the filing of the Information Disclosure Statement.

**Fees**

- ☒ No fee is owed by the applicant(s).  
☐ The **IDS Fee of \$180** under 37 CFR 1.17(p) is enclosed herewith.



In re Appln. of Kasid et al.  
Application No. 10/680,313

#### Method of Payment of Fees

- ☐ Attached is a check in the amount of \$ .  
☐ Charge Deposit Account No. 12-1216 in the amount of \$ . (A duplicate copy of this communication is enclosed for that purpose.)

#### Authorization to Charge Additional Fees

- ☒ If any additional fees are owed in connection with this communication, please charge Deposit Account No. 12-1216. (A duplicate copy of this communication is enclosed for that purpose.)

#### Instructions as to Overpayment

- ☒ Credit Account No. 12-1216.  
☐ Refund

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Date: May 26, 2005

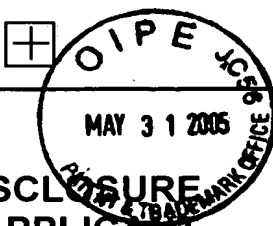
#### CERTIFICATE OF MAILING

I hereby certify that this INFORMATION DISCLOSURE STATEMENT (along with any documents referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to: Mail Stop , Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Date:

May 26, 2005

Please type a plus sign (+) inside this box →



Substitute for form 1449A/B/PTO

# **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

**Complete if Known**

|                        |                 |
|------------------------|-----------------|
| Application Number     | 10/680,313      |
| Filing Date            | October 6, 2003 |
| First Named Inventor   | Kasid et al.    |
| Group Art Unit         | 1635            |
| Examiner Name          | Schultz, James  |
| Attorney Docket Number | 224384          |

Sheet 1 of 8

## **U.S. PATENT DOCUMENTS**

| Examiner<br>Initials | Doc.<br>No. | U.S. Patent Document            |           | Name of Patentee or Applicant | Date of<br>Publication | Filing Date If<br>Appropriate |
|----------------------|-------------|---------------------------------|-----------|-------------------------------|------------------------|-------------------------------|
|                      |             | Application or<br>Patent Number | Kind Code |                               |                        |                               |
|                      | AD          | RE 30,985                       |           | Cartaya                       | June 29, 1982          |                               |
|                      | AE          | 4,399,216                       |           | Axel et al.                   | Aug. 16, 1983          |                               |
|                      | AF          | 4,551,433                       |           | DeBoer                        | Nov. 5, 1985           |                               |
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|                      | AH          | 4,657,866                       |           | Kumar                         | Apr. 14, 1987          |                               |
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|                      | AL          | 4,816,567                       |           | Cabilly et al.                | Mar. 28, 1989          |                               |
|                      | AM          | 4,837,148                       |           | Cregg                         | June 6, 1989           |                               |
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|                      | BA          | 5,422,120                       | A         | Kim                           | Jun. 6, 1995           |                               |
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|                      | BK          | 5,567,810                       | A         | Weis et al.                   | Oct. 22, 1996          |                               |
|                      | BL          | 5,571,799                       | A         | Tkachuk et al.                | Nov. 5, 1996           |                               |
|                      | BM          | 5,574,142                       | A         | Meyer, Jr. et al.             | Nov. 12, 1996          |                               |
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|--------------------------|----------|-------------------------|------------------------------|-----------|---|---------------------|-------------|----------------|
| Examiner Initials        | Doc. No. | Foreign Patent Document |                              |           | Name of Patentee or Applicant   | Date of Publication | Translation |                |
|                          |          | Office                  | Application or Patent Number | Kind Code |   |                     | Yes         | No**           |
|                          | CV       | WO                      | 87/00195                     | A1        | Celltech Limited  | Jan. 15, 1987       |             |                |
|                          | CW       | WO                      | 90/03430                     | A1        | Cetus Corporation   | Apr. 5, 1990        |             |                |
|                          | CX       | WO                      | 90/07936                     | A1        | Chiron Corporation  | Jul. 26, 1990       |             |                |
|                          | CY       | WO                      | 90/11092                     | A1        | Vical, Inc.   | Oct. 4, 1990        |             |                |
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|                          | DA       | WO                      | 91/02805                     | A2        | Viagene, Inc.   | Mar. 7, 1991        |             |                |
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|                          | DC       | WO                      | 91/14445                     | A1        | Research Development Foundation                                       | Oct. 3, 1991        |             |                |
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|                          | DJ       | WO                      | 93/09239                     | A1        | Research Corporation Technologies                                     | May 13, 1993        |             |                |
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|                          | DL       | WO                      | 93/11230                     | A1        | Dynal AS  | Jun. 10, 1993       |             |                |
|                          | DM       | WO                      | 93/19191                     | A1        | Centre National De LA Recherche Scientifique                          | Sep. 30, 1993       |             | X <sup>+</sup> |
|                          | DN       | WO                      | 93/25234                     | A1        | The Regents of the University of California                           | Dec. 23, 1993       |             |                |

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|  | DP | WO | 94/02602  | A1 | Cell Genesys, Inc.  | Feb. 3, 1994  |  |                |
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|  | DR | WO | 94/12649  | A2 | Genzyme Corporation   | Jun. 9, 1994  |  |                |
|  | DS | WO | 94/15645  | A1 | Texas Biotechnology Corporation                                       | Jul. 21, 1994 |  |                |
|  | DT | WO | 94/21792  | A2 | Viagene, Inc.   | Sep. 29, 1994 |  |                |
|  | DU | WO | 94/23697  | A1 | Depotech Corporation  | Oct. 27, 1994 |  |                |
|  | DV | WO | 94/28938  | A1 | The Regents of the University of Michigan                             | Dec. 22, 1994 |  |                |
|  | DW | WO | 95/00655  | A1 | Mc Master University  | Jan. 5, 1995  |  |                |
|  | DX | WO | 95/07994  | A2 | Viagene, Inc.   | Mar. 23, 1995 |  |                |
|  | DY | WO | 95/11984  | A2 | Canji, Inc.   | May 4, 1995   |  |                |
|  | DZ | WO | 95/13796  | A1 | Depotech Corporation  | May 26, 1995  |  |                |
|  | EA | WO | 95/27044  | A1 | Bioption AB   | Oct. 12, 1995 |  |                |
|  | EB | WO | 95/27069  | A1 | Smithkline Beecham Biologicals  | Oct. 12, 1995 |  |                |
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|  | ES | EP | 0 415 731 | A2 | The Wellcome Foundation Limited                                       | Mar. 6, 1991  |  |                |
|  | ET | EP | 0 524 968 | B1 | Depotech Corporation  | Feb. 3, 1993  |  |                |
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EW

OTHER - NON PATENT LITERATURE DOCUMENTS

| Examiner Initials | Doc. No. | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number (s), publisher, city and/or country where published. | Translation |                  |
|-------------------|----------|--|-------------|------------------|
|                   |          |  | Yes         | No <sup>++</sup> |
|                   | EW       | AGRAWAL, <i>Biochimica et Biophysica Acta</i> , 1489(1), 53-68 (1999)  |             |                  |
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| FK | BERTIN et al., <i>Proceedings of the National Academy of Sciences of the United States of America</i> , 94(4), 1172-1176 (1997)  |  |  |
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| KC  | LIM et al., <i>Gene</i> , 255, 35-42 (2000)  |  |  |
| KD  | LUCIAKOVA et al., <i>Biochemical Journal</i> , 352(2), 519-523 (2000)  |  |  |
| KE  | LUCKOW et al., <i>Bio/Technology</i> , 6(1), 47-55 (1988)  |  |  |
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| KN  | MILLER et al., <i>Genetic Engineering</i> , 8, 277-279 (1986) (Setlow et al. ed.)  |  |  |
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| KU  | MORRISON et al., <i>The Journal of Biological Chemistry</i> , 268(23), 17309-17316 (1993)  |  |  |
| KV  | MORRISON et al., <i>Proceedings of the National Academy of Sciences of the United States of America</i> , 81(21), 6851-6855 (1984)   |  |  |
| KW  | MORRISON et al., <i>Advances in Immunology</i> , 44, 65-92 (1988)  |  |  |
| KX  | MUZIO et al., <i>Cell</i> , 85(6), 817-827 (1996)  |  |  |
| KY  | NAKAI et al., <i>Genomics</i> , 14, 897-911 (1992)   |  |  |
| KZ  | NAKAMURA et al., <i>The Journal of Biological Chemistry</i> , 274(32), 22476-22483 (1999)  |  |  |
| LA  | NECKELMANN et al., <i>Proceedings of the National Academy of Sciences of the United States of America</i> , 84(21), 7580-7584 (1987) |  |  |
| LB  | NICOLETTI et al., <i>Journal of Immunological Methods</i> , 139(2), 271-279 (1991)   |  |  |
| LC  | ODA et al., <i>Biochemical and Biophysical Research Communications</i> , 193(3), 897-904 (1993)                                      |  |  |
| LD  | OHMICHII et al., <i>The Journal of Biological Chemistry</i> , 267(21), 14604-14610 (1992)  |  |  |
| LE  | OSTADE et al., <i>Nature</i> , 361(6409), 266-269 (1993)   |  |  |
| LF  | PADLAN et al., <i>Molecular Immunology</i> , 28(4/5), 489-498 (1991)   |  |  |
| LG  | PADLAN et al., <i>Molecular Immunology</i> , 31(3), 169-217 (1994)   |  |  |
| LH  | PATEL et al., <i>Molecular Carcinogenesis</i> , 18(1), 1-6 (1997)  |  |  |
| LI  | PATEL et al., <i>Oral Oncology</i> , 33(3), 197-203 (1997)   |  |  |
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| LM | PFEIFER et al., <i>Biochemical and Biophysical Research Communications</i> , 252(1), 481-486 (1998)                                 |  |  |
| LN | PHILIP, <i>Molecular and Cellular Biology</i> , 14(4), 2411-2418 (1994)   |  |  |
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| LP | PRASAD et al., <i>Molecular and Cellular Biology</i> , 12(11), 5260-5267 (1992)   |  |  |
| LQ | PULVERER et al., <i>Nature</i> , 353(6345), 670 (1991)  |  |  |
| LR | QURESHI et al., <i>The Journal of Biological Chemistry</i> , 266(31), 20594-20597 (1991)  |  |  |
| LS | RAM et al., <i>Cancer Research</i> , 53(1), 83-88 (1993)  |  |  |
| LT | RAPP et al., <i>The Oncogene Handbook</i> , (Elsevier Science Publishers, New York), 213-253 (1988)                                 |  |  |
| LU | RAPP, <i>Oncogene</i> , 6(4), 495-500 (1991)  |  |  |
| LV | REBAY et al., <i>Cell</i> , 67, 687-699 (1991)  |  |  |
| LW | REES et al., <i>The EMBO Journal</i> , 7(7), 2053-2061 (1988)   |  |  |
| LX | RIEDEL et al., <i>European Journal of Immunology</i> , 12, 3146-3150 (1993)   |  |  |
| LY | ROBBINS et al., <i>Diabetes</i> , 36(7), 838-845 (1987)   |  |  |
| LZ | ROGERS et al., <i>Genomics</i> , 39(2), 127-135 (1997)  |  |  |
| MA | ROGGENKAMP et al., <i>Molecular &amp; General Genetics</i> , 202(2), 302-308 (1986)   |  |  |
| MB | ROSENFELD et al., <i>Science</i> , 252(5004), 431-434 (1991)  |  |  |
| MC | SACCHI et al., <i>Archives of Otolaryngology-Head &amp; Neck Surgery</i> , 117(3), 321-326 (1991)                                   |  |  |
| MD | SAMUELS et al., <i>Molecular and Cellular Biology</i> , 13(10), 6241-6252 (1993)  |  |  |
| ME | SAMULSKI et al., <i>Journal of Virology</i> , 63(9), 3822-3828 (1989)   |  |  |
| MF | SARUBBI et al., <i>Analytical Biochemistry</i> , 237(1), 70-75 (1996)   |  |  |
| MG | SATA et al., <i>The Journal of Biological Chemistry</i> , 273(50), 33103-33106 (1998)   |  |  |
| MH | SCHAAP et al., <i>The Journal of Biological Chemistry</i> , 268(27), 20232-20236 (1993)   |  |  |
| MI | SCHNEIDER et al., <i>Tetrahedron Letters</i> , 31(3), 335-338 (1990)  |  |  |
| MJ | SETH et al., <i>The Journal of Biological Chemistry</i> , 266(35), 23521 (1991)   |  |  |
| MK | SIEBENLIST et al., <i>Cell</i> , 20(1), 269 (1980)  |  |  |
| ML | SIEGEL et al., <i>The Journal of Immunology</i> , 151(8), 4116-4127 (1993)  |  |  |
| MM | SMITH et al., <i>Proceedings of the National Academy of Sciences of the United States of America</i> , 82(24), 8404-8408 (1985)     |  |  |
| MN | SMITH et al., <i>Journal of Molecular Biology</i> , 224(4), 899-904 (1992)  |  |  |
| MO | SMITH et al., <i>Advances in Applied Mathematics</i> , 2(4), 482-489 (1981)   |  |  |
| MP | SOLDATENKOV et al., <i>The Cancer Journal from Scientific American</i> , 3(1), 13-20 (1997)   |  |  |
| MQ | SOZERI et al., <i>Oncogene</i> , 7(11), 2259 (1992)   |  |  |
| MR | SRINIVASULA et al., <i>The Journal of Biological Chemistry</i> , 272(30), 18542-18545 (1997)  |  |  |
| MS | STANTON et al., <i>Molecular and Cellular Biology</i> , 9(2), 639-647 (1989)  |  |  |
| MT | STEIN, <i>Biochimica et Biophysica Acta</i> , 1489(1), 45-52 (1999)   |  |  |
| MU | STENFLO, <i>Blood</i> , 78(7), 1637-1651 (1991)   |  |  |
| MV | STOKOE et al., <i>The EMBO Journal</i> , 11(11), 3985-3994 (1992)   |  |  |
| MW | STURGILL et al., <i>Nature</i> , 334(6184), 715-718 (1988)  |  |  |
| MX | SUN et al., <i>Hepatology</i> , 27(1), 228-239 (1998)   |  |  |
| MY | SUNNERHAGEN et al., <i>The Journal of Biological Chemistry</i> , 268(31), 2339-2344 (1993)  |  |  |
| MZ | SUY et al., <i>Oncogene</i> , 15(1), 53-61 (1997)   |  |  |
| NA | TAKAMIYA et al., <i>Journal of Neuroscience Research</i> , 33(3), 493-503 (1992)  |  |  |
| NB | TEWARI et al., <i>The Journal of Biological Chemistry</i> , 270(39), 22705-22708 (1995)   |  |  |
| NC | THOME et al., <i>Nature</i> , 386(6624), 517-521 (1997)   |  |  |
| ND | TILBURN et al., <i>Gene</i> , 26(2&3), 205-221 (1983)   |  |  |
| NE | TORNKVIST et al., <i>The Journal of Biological Chemistry</i> , 269(19), 13919-13921 (1994)  |  |  |
| NF | TRAVERSE et al., <i>Oncogene</i> , 8(11), 3175-3181 (1993)  |  |  |
| NG | TROPPEMAIR et al., <i>Mechanisms in B-Cell Neoplasia 1992</i> , 453-460 (1992)  |  |  |
| NH | TURNER et al., <i>Proceedings of the National Academy of Sciences of the United States of America</i> , 90(12), 5544-5548 (1993)    |  |  |
| NI | UHLMANN et al., <i>Chemical Reviews</i> , 90(4), 543-584 (1990)   |  |  |
| NJ | VAN DEN BERG et al., <i>Bio/Technology</i> , 8(2), 135139 (1990)  |  |  |
| NK | VERHOEYER et al., <i>Science</i> , 239(4847), 1534-1536 (1988)  |  |  |
| NL | VILE et al., <i>Cancer Research</i> , 53(5), 962-967 (1993)   |  |  |





School of Law

December 30, 2003

Re: U.S. Patent Application No. 10/443,273  
Prafulla Gokhale et al., "Gene BRCC-1 and diagnostic and  
therapeutic uses thereof," Attorney Docket No. 222359

Prafulla Gokhale, Inventor  
c/o Leydig, Voit & Mayer, Ltd.  
Two Prudential Plaza, Suite 4900  
180 North Stetson Avenue  
Chicago, IL 60601-6780

Dear Mr. Gokhale:

I am writing to call your attention to a printed publication that may constitute material prior art with respect to the above-referenced patent application.

Enclosed please find a copy of a CD-ROM document entitled "On the preparation and utilization of isolated and purified oligonucleotides," which I produced on March 9, 2002 and contributed to the public collection of the Kathrine R. Everett Law Library of the University of North Carolina on March 14, 2002.

For your convenience, I have also enclosed a hard copy of the initial portion of the text file stored on that CD-ROM. As you can ascertain from that excerpt, the CD-ROM reference contains a full written description of several million oligonucleotides of between 8 and 12 nucleotides in length inclusive, together with methods of making and using each.

I believe that the reference is material prior art at least with respect to one or more claims of the above-referenced application. Accordingly, I would recommend that the attorney or agent handling this application promptly disclose this reference to the Patent Office. As a courtesy, I would appreciate a written acknowledgement that he or she has done so.

If you wish to discuss this matter, I can be reached at the above phone number or by email at chin@unc.edu.

Sincerely yours,

Andrew Chin  
Associate Professor

## On the Preparation and Utilization of Isolated and Purified Oligonucleotides

Andrew Chin

University of North Carolina School of Law

March 9, 2002

The term "isolated" as used herein refers to a nucleotide sequence that has been manually produced and is separated from its native, in vivo, cellular environment and is present in the substantial absence of other biological molecules of the same type. The term "purified" as used herein for nucleotide sequences preferably means lacking significant quantities of other biological macromolecules of the same type (but water, buffers, and other small molecules, can be present).

### Preparation of Isolated and Purified Oligonucleotides

As described in U.S. Patent No. 5,808,022 (issued Sept. 15, 1998) (William D. Huse), oligonucleotide synthesis proceeds via linear coupling of individual monomers in a stepwise reaction. The reactions are generally performed on a solid phase support by first coupling the 3' end of the first monomer to the support. The second monomer is added to the 5' end of the first monomer in a condensation reaction to yield a dinucleotide coupled to the solid support. At the end of each coupling reaction, the by-products and unreacted, free monomers are washed away so that the starting material for the next round of synthesis is the pure oligonucleotide attached to the support. In this reaction scheme, the stepwise addition of individual monomers to a single, growing end of an oligonucleotide ensures accurate synthesis of the desired sequence. Moreover, unwanted side reactions are eliminated, such as the condensation of two oligonucleotides, resulting in high product yields.

Oligonucleotides are constructed by conventional procedures such as those described in J. Sambrook et al., *Molecular Cloning: A Laboratory Manual* 10.42-.46 (3rd ed. 2001); K. Itakura et al., *Synthesis and Use of Synthetic Oligonucleotides*, 53 *Ann. Rev. Biochemistry* 323 (1984); M.D. Matteucci & M.H. Caruthers, *Synthesis of Deoxynucleotides on a Polymer Support*, 103 *J. Am. Chem. Soc.* 3185 (1981); S.A. Narang, *DNA Synthesis*, 39 *Tetrahedron* 3 (1983). Oligonucleotide chains up to about 70 nucleotide residues long are preferably synthesized on automated synthesizers well known in the art (such as the Beckman Oligo 1000 or the Applied Biosystems ABI 392 DNA Synthesizer). Present-day DNA synthesizers are so efficient that oligonucleotides up to about 25 nucleotides in length generally do not contain significant quantities of truncated DNA fragments and hence do not require purification by gel electrophoresis. If necessary, however, purification of synthetic oligonucleotides can be achieved by one of several methods, as described in J. Sambrook, *supra*, at 10.48-49; including denaturing polyacrylamide gel electrophoresis, as described in J. Sambrook, *supra*, at 10.11-.16; T. Atkinson & M. Smith, *Solid-Phase Synthesis of Oligodeoxyribonucleotides by the Phosphate-Triester Method*, in *Oligonucleotide Synthesis: A Practical Approach* 35-82 (M.J. Gait ed. 1984).

### Utilization of Oligonucleotides

As described in U.S. Patent No. 6,316,191 (issued Nov. 13, 2001) (Radoje T. Drmanac), hybridization depends on the pairing of complementary bases in nucleic acids and is a specific tool useful for the general recognition of informational polymers. Diverse research problems using hybridization of a synthetic oligonucleotide of known sequence include, amongst others, the different techniques of identification of specific clones from cDNA and genomic libraries, detecting single base pair polymorphisms in DNA, generation of mutations by oligonucleotide mutagenesis, and the amplification of nucleic acids in vitro from a single sperm, an extinct organism, or a single virus infecting a single cell.

Synthetic oligonucleotides of arbitrary nucleotide sequence are utilized in biological research, wherein oligonucleotides of specified length and random nucleotide sequence are synthesized using known procedures such as those described in Huse, *supra*; U.S. Patent No. 5,639,595 (issued June 17, 1997) (Christopher K. Mirabelli et al.). Arbitrary oligonucleotide primers of specified length may be used in the synthesis of cDNA probes from mRNA as described in Sambrook, *supra*, at 9.38-.40; J.G. Williams et al., DNA Polymorphisms Amplified By Arbitrary Primers Are Useful As Genetic Markers, 18 Nucleic Acids Research 6531 (1990), in the systematic evolution of ligands by exponential enrichment as described in U.S. Patent No. 6,331,398 (issued Dec. 18, 2001) (Larry Gold & Craig Tuerk); C. Tuerk & L. Gold, Systematic Evolution of High-Affinity RNA Ligands of Bacteriophage T4 DNA Polymerase in Vitro, 249 Science 505 (1990), and in sequencing by hybridization as described in Drmanac, *supra*. Preferably, oligonucleotide primers and probes are characterized by sequences of 8 to 20 nucleotides that have moderate G+C content, are free of homopolymeric runs and directly or inversely repeated regions.

The disclosures of all publications and patents set forth hereinbefore are expressly incorporated herein by reference.

#### Sequence Listing

The listing of sequences set forth hereinafter consists of all sequences of 8 to 12 nucleotides that have between 40 and 60 percent G+C content and are free of homopolymeric runs of 4 or more bases and directly or inversely repeated regions of 4 or more bases. Based on the the disclosures herein and the knowledge of a person of ordinary skill in the art, it will be apparent to such a person how to make and use an isolated and/or purified oligonucleotide characterized by any of the following nucleotide sequences: